


## PCT

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference PHM 70390/WO	<b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/GB99/03071	International filing date (day/month/year) 15/09/1999	Priority date (day/month/year) 19/09/1998
International Patent Classification (IPC) or national classification and IPC C12Q1/68		
Applicant ASTRAZENECA AB		
<p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 8 sheets, including this cover sheet.</p> <p><input type="checkbox"/> This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of sheets.</p>		
<p>3. This report contains indications relating to the following items:</p> <p>I <input checked="" type="checkbox"/> Basis of the report</p> <p>II <input type="checkbox"/> Priority</p> <p>III <input checked="" type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</p> <p>IV <input type="checkbox"/> Lack of unity of invention</p> <p>V <input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p>VI <input type="checkbox"/> Certain documents cited</p> <p>VII <input checked="" type="checkbox"/> Certain defects in the international application</p> <p>VIII <input checked="" type="checkbox"/> Certain observations on the international application</p>		
Date of submission of the demand  17/03/2000	Date of completion of this report  05.12.2000	
Name and mailing address of the international preliminary examining authority:   European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer  Weaver, M  Telephone No. +49 89 2399 8689	



**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/GB99/03071

**I. Basis of the report**

1. This report has been drawn on the basis of *(substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments (Rules 70.16 and 70.17).):*

**Description, pages:**

1-25 as originally filed

**Claims, No.:**

1-11 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

# INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB99/03071

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

### III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application.
- ☒ claims Nos. 6.

because:

- ☒ the said international application, or the said claims Nos. 6 relate to the following subject matter which does not require an international preliminary examination (*specify*):  
**see separate sheet**
- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- ☐ no international search report has been established for the said claims Nos. .

2. A meaningful international preliminary examination report cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

- ☐ the written form has not been furnished or does not comply with the standard.
- ☐ the computer readable form has not been furnished or does not comply with the standard.

### V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims 1-5, 7-11
	No: Claims
Inventive step (IS)	Yes: Claims
	No: Claims 1-5, 7-11
Industrial applicability (IA)	Yes: Claims 1-5, 7-11

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/GB99/03071

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No: Claims

2. Citations and explanations  
**see separate sheet**

**VII. Certain defects in the international application**

The following defects in the form or contents of the international application have been noted:  
**see separate sheet**

**VIII. Certain observations on the international application**

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:  
**see separate sheet**

## **Section I**

Sequence listing pages 1 - 3 have also been taken into account for the purposes of this Report.

## **Section III**

Claim 6 is directed to a computer-readable medium having at least one nucleic acid sequence of claim 5 stored thereon. This is, however, nothing more than a representation of information, i.e. a record of the polymorphisms listed in claim 5 in the form of e.g. a diskette, a hard drive or magnetic computer tape on which one or more polynucleotide sequences is stored. It should be noted that the computer-readable medium itself does not comprise new technical features. Claim 6 will thus not be the subject of international preliminary examination (Rule 67.1(v) PCT and the Guidelines Ch. IV-2.4(e)).

## **Section V**

1. D1 (Molec Immunol 32 (1996) 1453; page 1453, lines 8 - 10, 45 - 49; Figure 1) discloses a single nucleotide polymorphism (SNP) in the human  $\alpha 4$  integrin subunit coding sequence, at position 3061 in Figure 1 of D1, and several differences in the 5'-3' untranslated regions. It would appear from the disclosure of D1 that the coding SNP relates to variants found in the normal population that do not result in any functional abnormality of the gene product.
2. The subject-matter of claim 1 of the present application, insofar as it relates to SNPs in the human  $\alpha 4$  integrin subunit coding sequence, differs from the disclosure of D1 in that the SNPs are in different positions within the coding sequence.

As there is no evidence in the application as filed that the coding sequence SNPs of claim 1 are associated in any way with a functional abnormality in the gene, the problem to be solved can only be formulated as the provision of means for determining the  $\alpha 4$  integrin subunit "status" of a subject (see wording of claim 1).

This problem is solved by the provision of a method for determining SNPs at specific locations within the coding sequence of the  $\alpha 4$  integrin subunit gene.

However, D1 clearly discloses that the human  $\alpha 4$  integrin subunit gene contains at least one SNP. It would thus be obvious for the skilled person to determine whether other SNPs existed, when seeking to solve the problem posed. He would be able to achieve this goal by employing one of the many techniques known in the art for this purpose, such as ARMS (see e.g. D2 Nucl Acids Res 17 (1989) 2503).

Similar arguments apply to the remaining subject-matter of claim 1 directed to SNPs in the promoter region, additionally given that D3 (J Biol Chem 269 (1994) 15652; page 15652, column 2, paragraph 5 - page 15653, column 1, paragraph 5; page 15657, column 2, paragraph 2 - page 15658, column 1, paragraph 1, Figure 7) discloses that point mutations in the promoter region are associated with loss of transcription of the human  $\alpha 4$  integrin subunit gene. This would thus represent an even greater incentive for the skilled person to investigate the existence of further SNPs in the promoter region of the gene.

Claim 1 thus lacks an inventive step and does not meet the requirements of Article 33(3) PCT.

3. Dependent claims 2 - 4 do not contain any features which, in combination with the features of any claim to which they refer, meet the requirements of the PCT in respect of inventive step, given the disclosures of D1 - D3.

These claims also do not meet the requirements of Article 33(3) PCT.

4. Claims 5, 7 and 8 are dependent on the existence of the further SNPs referred to in claim 1 and thus lack an inventive step over the disclosures of D1 and D3 for similar reasons to those given in point 2 (Article 33(3) PCT).
5. The allelic variant of the human  $\alpha 4$  integrin subunit of claim 9 presumably arises as a result of one of the SNPs referred to in claim 1, although this is not specifically indicated in the application as filed. Nevertheless, as this variant does

not appear to be associated with any particular functional abnormality of the subunit, there can be nothing inventive associated with such variants, given that the identification of the SNP which gives rise to the variant is considered to lack an inventive step for the reasons set out in point 2 above.

Claim 9 thus does not meet the requirements of Article 33(3) PCT.

6. The association of the SNPs listed in claim 10 with an  $\alpha 4$  integrin subunit ligand mediated disease in humans has neither been disclosed nor demonstrated in the application as filed (see Section VIII below).

Nevertheless, even if such an association had been demonstrated, use of an  $\alpha 4$  integrin subunit ligand antagonist drug in the treatment of an  $\alpha 4$  integrin subunit ligand mediated disease associated with the non-inventive SNPs of claim 10 would also lack an inventive step, given that such drugs are known in the art (see e.g. D4 Curr Opin Chem Biol 2 (1998) 453; abstract; page 453, column 2, line 1 - page 456, column 1, line 49) and D5 (Nature 356 (1992) 63).

Similar arguments apply to the subject-matter of claim 11, which is directed to the use of the non-inventive SNP-containing sequences of claim 5 to determine whether a compound is e.g. an  $\alpha 4$  integrin subunit ligand antagonist.

Claims 10 and 11 therefore do not meet the requirements of Article 33(3) PCT.

7. For the assessment of the present claim 10 on the question whether it is industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

## **Section VII**

Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art

disclosed in the documents D1, D2 and D5 is not mentioned in the description, nor are these documents identified therein.

### **Section VIII**

1. There is a discrepancy between the EMBL ACCESSION NOs given on page 3, lines 14/15 and those used in the claims (Article 6 PCT and the PCT Guidelines Ch. III-4.3).
2. Claims 1 - 4 lack clarity (Article 6 PCT) as they refer to a method for **diagnosis**, although no disease is diagnosed simply by performing the methods of these claims.
3. Claims 7 , 8 and 10 lack clarity (Article 6 PCT), as the word "positions" appears twice consecutively at several points (e.g. lines 2 and 3 of claim 7).
4. Claims 10 and 11 are not sufficiently disclosed as required by Article 5 PCT, as there is no indication or evidence in the application as filed with respect to whether any of the indicated SNPs are actually associated with any disease nor how the skilled person should attempt to identify any such disease.



# PCT

## REQUEST

The undersigned requests that the present international application be processed according to the Patent Cooperation Treaty.

For receiving Office use only

International Application No.

International Filing Date

Name of receiving Office and "PCT International Application"

Applicant's or agent's file reference  
(if desired) (12 characters maximum) PHM 70390/WO

<b>Box No. I TITLE OF INVENTION</b> CHEMICAL COMPOUNDS	
<b>Box No. II APPLICANT</b>	
Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)	
ZENECA Limited 15 Stanhope Gate LONDON GB-W1Y 6LN GB	<input type="checkbox"/> This person is also inventor. Telephone No. (01625) 516173 Facsimile No. (01625) 583358 Teleprinter No. 669095/669388
State (that is, country) of nationality: GB	State (that is, country) of residence: GB
This person is applicant for the purposes of: <input type="checkbox"/> all designated States <input checked="" type="checkbox"/> all designated States except the United States of America <input type="checkbox"/> the United States of America only <input type="checkbox"/> the States indicated in the Supplemental Box	
<b>Box No. III FURTHER APPLICANT(S) AND/OR (FURTHER) INVENTOR(S)</b>	
Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)	
MORTEN, John Edward Norris Alderley Park Macclefield Cheshire GB-SK10 4TG GB	This person is: <input type="checkbox"/> applicant only <input checked="" type="checkbox"/> applicant and inventor <input type="checkbox"/> inventor only (If this check-box is marked, do not fill in below.)
State (that is, country) of nationality: GB	State (that is, country) of residence: GB
This person is applicant for the purposes of: <input type="checkbox"/> all designated States <input type="checkbox"/> all designated States except the United States of America <input checked="" type="checkbox"/> the United States of America only <input type="checkbox"/> the States indicated in the Supplemental Box	
<input type="checkbox"/> Further applicants and/or (further) inventors are indicated on a continuation sheet.	
<b>Box No. IV AGENT OR COMMON REPRESENTATIVE; OR ADDRESS FOR CORRESPONDENCE</b>	
The person identified below is hereby/has been appointed to act on behalf of the applicant(s) before the competent International Authorities as: <input checked="" type="checkbox"/> agent <input type="checkbox"/> common representative	
Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)	
GILES, Allen Frank Global Intellectual Property ASTRAZENECA PLC Mereside, Alderley Park Macclesfield, Cheshire, GB-SK10 4TG, GB	Telephone No. (01625) 516573 Facsimile No. (01625) 583358 Teleprinter No. 669095/669388
<input type="checkbox"/> Address for correspondence: Mark this check-box where no agent or common representative is/has been appointed and the space above is used instead to indicate a special address to which correspondence should be sent.	

**Box No.V DESIGNATION OF STATES**

The following designations are hereby made under Rule 4.9(a) (mark the applicable check-boxes; at least one must be marked):

**Regional Patent**

- ☒ **AP ARIPO Patent:** GH Ghana, GM Gambia, KE Kenya, LS Lesotho, MW Malawi, SD Sudan, SZ Swaziland, UG Uganda, ZW Zimbabwe, and any other State which is a Contracting State of the Harare Protocol and of the PCT
- ☒ **EA Eurasian Patent:** AM Armenia, AZ Azerbaijan, BY Belarus, KG Kyrgyzstan, KZ Kazakhstan, MD Republic of Moldova, RU Russian Federation, TJ Tajikistan, TM Turkmenistan, and any other State which is a Contracting State of the Eurasian Patent Convention and of the PCT
- ☒ **EP European Patent:** AT Austria, BE Belgium, CH and LI Switzerland and Liechtenstein, CY Cyprus, DE Germany, DK Denmark, ES Spain, FI Finland, FR France, GB United Kingdom, GR Greece, IE Ireland, IT Italy, LU Luxembourg, MC Monaco, NL Netherlands, PT Portugal, SE Sweden, and any other State which is a Contracting State of the European Patent Convention and of the PCT
- ☒ **OA OAPI Patent:** BF Burkina Faso, BJ Benin, CF Central African Republic, CG Congo, CI Côte d'Ivoire, CM Cameroon, GA Gabon, GN Guinea, GW Guinea-Bissau, ML Mali, MR Mauritania, NE Niger, SN Senegal, TD Chad, TG Togo, and any other State which is a member State of OAPI and a Contracting State of the PCT (if other kind of protection or treatment desired, specify on dotted line) .....

**National Patent** (if other kind of protection or treatment desired, specify on dotted line):

- |  |  |
|--|--|
| <input checked="" type="checkbox"/> AL Albania .....                               | <input checked="" type="checkbox"/> LS Lesotho .....                                   |
| <input checked="" type="checkbox"/> AM Armenia .....                               | <input checked="" type="checkbox"/> LT Lithuania .....                                 |
| <input checked="" type="checkbox"/> AT Austria .....                               | <input checked="" type="checkbox"/> LU Luxembourg .....                                |
| <input checked="" type="checkbox"/> AU Australia .....                             | <input checked="" type="checkbox"/> LV Latvia .....                                    |
| <input checked="" type="checkbox"/> AZ Azerbaijan .....                            | <input checked="" type="checkbox"/> MD Republic of Moldova .....                       |
| <input checked="" type="checkbox"/> BA Bosnia and Herzegovina .....                | <input checked="" type="checkbox"/> MG Madagascar .....                                |
| <input checked="" type="checkbox"/> BB Barbados .....                              | <input checked="" type="checkbox"/> MK The former Yugoslav Republic of Macedonia ..... |
| <input checked="" type="checkbox"/> BG Bulgaria .....                              | <input checked="" type="checkbox"/> MN Mongolia .....                                  |
| <input checked="" type="checkbox"/> BR Brazil .....                                | <input checked="" type="checkbox"/> MW Malawi .....                                    |
| <input checked="" type="checkbox"/> BY Belarus .....                               | <input checked="" type="checkbox"/> MX Mexico .....                                    |
| <input checked="" type="checkbox"/> CA Canada .....                                | <input checked="" type="checkbox"/> NO Norway .....                                    |
| <input checked="" type="checkbox"/> CH and LI Switzerland and Liechtenstein .....  | <input checked="" type="checkbox"/> NZ New Zealand .....                               |
| <input checked="" type="checkbox"/> CN China .....                                 | <input checked="" type="checkbox"/> PL Poland .....                                    |
| <input checked="" type="checkbox"/> CU Cuba .....                                  | <input checked="" type="checkbox"/> PT Portugal .....                                  |
| <input checked="" type="checkbox"/> CZ Czech Republic .....                        | <input checked="" type="checkbox"/> RO Romania .....                                   |
| <input checked="" type="checkbox"/> DE Germany .....                               | <input checked="" type="checkbox"/> RU Russian Federation .....                        |
| <input checked="" type="checkbox"/> DK Denmark .....                               | <input checked="" type="checkbox"/> SD Sudan .....                                     |
| <input checked="" type="checkbox"/> EE Estonia .....                               | <input checked="" type="checkbox"/> SE Sweden .....                                    |
| <input checked="" type="checkbox"/> ES Spain .....                                 | <input checked="" type="checkbox"/> SG Singapore .....                                 |
| <input checked="" type="checkbox"/> FI Finland .....                               | <input checked="" type="checkbox"/> SI Slovenia .....                                  |
| <input checked="" type="checkbox"/> GB United Kingdom .....                        | <input checked="" type="checkbox"/> SK Slovakia .....                                  |
| <input checked="" type="checkbox"/> GD Grenada .....                               | <input checked="" type="checkbox"/> SL Sierra Leone .....                              |
| <input checked="" type="checkbox"/> GE Georgia .....                               | <input checked="" type="checkbox"/> TJ Tajikistan .....                                |
| <input checked="" type="checkbox"/> GH Ghana .....                                 | <input checked="" type="checkbox"/> TM Turkmenistan .....                              |
| <input checked="" type="checkbox"/> GM Gambia .....                                | <input checked="" type="checkbox"/> TR Turkey .....                                    |
| <input checked="" type="checkbox"/> HR Croatia .....                               | <input checked="" type="checkbox"/> TT Trinidad and Tobago .....                       |
| <input checked="" type="checkbox"/> HU Hungary .....                               | <input checked="" type="checkbox"/> UA Ukraine .....                                   |
| <input checked="" type="checkbox"/> ID Indonesia .....                             | <input checked="" type="checkbox"/> UG Uganda .....                                    |
| <input checked="" type="checkbox"/> IL Israel .....                                | <input checked="" type="checkbox"/> US United States of America .....                  |
| <input checked="" type="checkbox"/> IN India .....                                 | <input checked="" type="checkbox"/> UZ Uzbekistan .....                                |
| <input checked="" type="checkbox"/> IS Iceland .....                               | <input checked="" type="checkbox"/> VN Viet Nam .....                                  |
| <input checked="" type="checkbox"/> JP Japan .....                                 | <input checked="" type="checkbox"/> YU Yugoslavia .....                                |
| <input checked="" type="checkbox"/> KE Kenya .....                                 | <input checked="" type="checkbox"/> ZW Zimbabwe .....                                  |
| <input checked="" type="checkbox"/> KG Kyrgyzstan .....                            |  |
| <input checked="" type="checkbox"/> KP Democratic People's Republic of Korea ..... |  |
| <input checked="" type="checkbox"/> KR Republic of Korea .....                     |  |
| <input checked="" type="checkbox"/> KZ Kazakhstan .....                            |  |
| <input checked="" type="checkbox"/> LC Saint Lucia .....                           |  |
| <input checked="" type="checkbox"/> LK Sri Lanka .....                             |  |
| <input checked="" type="checkbox"/> LR Liberia .....                               |  |

Check-boxes reserved for designating States (for the purposes of a national patent) which have become party to the PCT after issuance of this sheet:

- ☒ DM Dominica .....
- ☒ AE United Arab Emirates .....
- ☒ ZA South Africa .....
- ☒ CR Costa Rica .....

**Precautionary Designation Statement:** In addition to the designations made above, the applicant also makes under Rule 4.9(b) all other designations which would be permitted under the PCT except any designation(s) indicated in the Supplemental Box as being excluded from the scope of this statement. The applicant declares that those additional designations are subject to confirmation and that any designation which is not confirmed before the expiration of 15 months from the priority date is to be regarded as withdrawn by the applicant at the expiration of that time limit. (Confirmation of a designation consists of the filing of a notice specifying that designation and the payment of the designation and confirmation fees. Confirmation must reach the receiving Office within the 15-month time limit.)

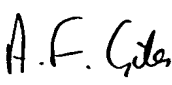
<b>Box No. VI PRIORITY CLAIM</b>					<input type="checkbox"/> Further priority claim indicated in the Supplemental Box.
Filing date of earlier application (day/month/year)	Number of earlier application	Where earlier application is:			
		national application: country	regional application:* regional Office	international application: receiving Office	
item (1) 19-Sep-98 (19.09.98)	9820339.1	GB			
item (2) 10-Nov-98 (10.11.98)	9824506.1	GB			
item (3)					

☐ The receiving Office is requested to prepare and transmit to the International Bureau a certified copy of the earlier application(s) (only if the earlier application was filed with the Office which for the purposes of the present international application is the receiving Office) identified above as item(s): \_\_\_\_\_

\* Where the earlier application is an ARIPO application, it is mandatory to indicate in the Supplemental Box at least one country party to the Paris Convention for the Protection of Industrial Property for which that earlier application was filed (Rule 4.10(b)(ii)). See Supplemental Box.

<b>Box No. VII INTERNATIONAL SEARCHING AUTHORITY</b>			
<b>Choice of International Searching Authority (ISA)</b> (if two or more International Searching Authorities are competent to carry out the international search, indicate the Authority chosen; the two-letter code may be used): ISA /		<b>Request to use results of earlier search; reference to that search</b> (if an earlier search has been carried out by or requested from the International Searching Authority): Date (day/month/year)      Number      Country (or regional Office)	

<b>Box No. VIII CHECK LIST; LANGUAGE OF FILING</b>	
This international application contains the following number of sheets: request : 4 description (excluding sequence listing part) : 30 claims : 4 abstract : 1 drawings : sequence listing part of description : 3 Total number of sheets : 42	This international application is accompanied by the item(s) marked below: 1. <input checked="" type="checkbox"/> fee calculation sheet 2. <input checked="" type="checkbox"/> separate signed power of attorney 3. <input type="checkbox"/> copy of general power of attorney; reference number, if any: 4. <input type="checkbox"/> statement explaining lack of signature 5. <input type="checkbox"/> priority document(s) identified in Box No. VI as item(s): 6. <input type="checkbox"/> translation of international application into (language): 7. <input type="checkbox"/> separate indications concerning deposited microorganism or other biological material 8. <input checked="" type="checkbox"/> nucleotide and/or amino acid sequence listing in computer readable form 9. <input type="checkbox"/> other (specify):
Figure of the drawings which should accompany the abstract:	Language of filing of the international application: <b>ENGLISH</b>

<b>Box No. IX SIGNATURE OF APPLICANT OR AGENT</b>	
Next to each signature, indicate the name of the person signing and the capacity in which the person signs (if such capacity is not obvious from reading the request). <div style="text-align: center; margin-top: 20px;">   <b>GILES, Allen Frank</b>  <b>AGENT FOR APPLICANT</b> </div>	

For receiving Office use only		2. Drawings:  <input type="checkbox"/> received:  <input type="checkbox"/> not received:
1. Date of actual receipt of the purported international application:		
3. Corrected date of actual receipt due to later but timely received papers or drawings completing the purported international application:		
4. Date of timely receipt of the required corrections under PCT Article 11(2):		
5. International Searching Authority (if two or more are competent): <b>ISA /</b>	6. <input type="checkbox"/> Transmittal of search copy delayed until search fee is paid.	

For International Bureau use only
Date of receipt of the record copy by the International Bureau:

# PCT

## FEE CALCULATION SHEET Annex to the Request

For receiving Office use only

International application No.

Date stamp of the receiving Office

Applicant's or agent's  
file reference

Applicant

### CALCULATION OF PRESCRIBED FEES

1. TRANSMITTAL FEE . . . . .  T

2. SEARCH FEE . . . . .  S

International search to be carried out by \_\_\_\_\_  
(If two or more International Searching Authorities are competent in relation to the international application, indicate the name of the Authority which is chosen to carry out the international search.)

3. INTERNATIONAL FEE

#### Basic Fee

The international application contains \_\_\_\_\_ sheets.

first 30 sheets . . . . .  b1

\_\_\_\_\_ x \_\_\_\_\_ =  b2  
remaining sheets additional amount

Add amounts entered at b1 and b2 and enter total at B . . . . .  B

#### Designation Fees

The international application contains \_\_\_\_\_ designations.

\_\_\_\_\_ x \_\_\_\_\_ =  D  
number of designation fees amount of designation fee  
payable (maximum 10)

Add amounts entered at B and D and enter total at I . . . . .  I

(Applicants from certain States are entitled to a reduction of 75% of the international fee. Where the applicant is (or all applicants are) so entitled, the total to be entered at I is 25% of the sum of the amounts entered at B and D.)

4. FEE FOR PRIORITY DOCUMENT (if applicable) . . . . .  P

5. TOTAL FEES PAYABLE . . . . .

Add amounts entered at T, S, I and P, and enter total in the TOTAL box

TOTAL

☐ The designation fees are not paid at this time.

### MODE OF PAYMENT

☐ authorization to charge  
deposit account (see below)

☐ bank draft

☐ coupons

☐ cheque

☐ cash

☐ other (specify):

☐ postal money order

☐ revenue stamps

### DEPOSIT ACCOUNT AUTHORIZATION (this mode of payment may not be available at all receiving Offices)

The RO/ \_\_\_\_\_ ☐ is hereby authorized to charge the total fees indicated above to my deposit account.

☐ (this check-box may be marked only if the conditions for deposit accounts of the receiving Office so permit) is hereby authorized to charge any deficiency or credit any overpayment in the total fees indicated above to my deposit account.

☐ is hereby authorized to charge the fee for preparation and transmittal of the priority document to the International Bureau of WIPO to my deposit account.

Deposit Account No.

Date (day/month/year)

Signature

## PATENT COOPERATION TREATY

COPY TO DEB

From the INTERNATIONAL BUREAU

To:

GILES, Allen, Frank  
AstraZeneca  
Global Intellectual Property  
P.O. Box 272  
Mereside, Alderley Park  
Macclesfield, Cheshire SK10 4GR  
ROYAUME-UNI

NOTIFICATION OF THE RECORDING  
OF A CHANGE

(PCT Rule 92bis.1 and  
Administrative Instructions, Section 422)

Date of mailing (day/month/year)  
28 September 2000 (28.09.00)

Applicant's or agent's file reference  
PHM 70390/WO

International application No.  
PCT/GB99/03071

## IMPORTANT NOTIFICATION

International filing date (day/month/year)  
15 September 1999 (15.09.99)

## 1. The following indications appeared on record concerning:

☒ the applicant ☐ the inventor ☐ the agent ☐ the common representative

## Name and Address

ASTRAZENECA UK LIMITED  
15 Stanhope Gate  
London W1Y 6LN  
United Kingdom

State of Nationality  
GB

State of Residence  
GB

Telephone No.

Facsimile No.

Teleprinter No.

## 2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

☒ the person ☒ the name ☒ the address ☒ the nationality ☒ the residence

## Name and Address

ASTRAZENECA AB *SK*  
S-151 85 Södertälje  
Sweden

State of Nationality  
SE

State of Residence  
SE

Telephone No.

Facsimile No.

Teleprinter No.

## 3. Further observations, if necessary:

## 4. A copy of this notification has been sent to:

☒ the receiving Office ☐ the designated Offices concerned  
☐ the International Searching Authority ☒ the elected Offices concerned  
☒ the International Preliminary Examining Authority ☐ other:

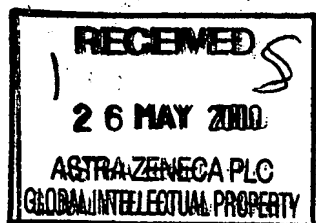
The International Bureau of WIPO  
34, chemin des Colombettes  
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer

Athina Nickitas-Etienne *AN*

Telephone No.: (41-22) 338.83.38



## PATENT COOPERATION TREATY

PCT

From the INTERNATIONAL BUREAU

To:

GILES, Allen, Frank  
AstraZeneca UK Limited  
Global Intellectual Property  
Mereside, Alderley Park  
Macclesfield  
Cheshire SK10 4TG  
ROYAUME-UNI

NOTIFICATION OF THE RECORDING  
OF A CHANGE

(PCT Rule 92bis.1 and  
Administrative Instructions, Section 422)

Date of mailing (day/month/year) 10 May 2000 (10.05.00)	<b>IMPORTANT NOTIFICATION</b>
Applicant's or agent's file reference PHM 70390/WO	
International application No. PCT/GB99/03071	International filing date (day/month/year) 15 September 1999 (15.09.99)

## 1. The following indications appeared on record concerning:

☒ the applicant ☐ the inventor ☐ the agent ☐ the common representative

## Name and Address

ZENECA LIMITED  
15 Stanhope Gate  
London W1Y 6LN  
United Kingdom

## State of Nationality

GB

## State of Residence

GB

Telephone No.

Facsimile No.

Teleprinter No.

## 2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

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## Name and Address

ASTRAZENECA UK LIMITED  
15 Stanhope Gate  
London W1Y 6LN  
United Kingdom

## State of Nationality

GB

## State of Residence

GB

Telephone No.

Facsimile No.

Teleprinter No.

## 3. Further observations, if necessary:

Please note that the change of applicant's name applies also for the agent's address.

## 4. A copy of this notification has been sent to:

☒ the receiving Office ☐ the designated Offices concerned  
☐ the International Searching Authority ☒ the elected Offices concerned  
☒ the International Preliminary Examining Authority ☐ other:

The International Bureau of WIPO  
34, chemin des Colombettes  
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer

  
Mougamadou ABIDINE

Telephone No.: (41-22) 338.83.38

## PATENT COOPERATION TREATY

PCT

## NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Assistant Commissioner for Patents  
United States Patent and Trademark  
Office  
Box PCT  
Washington, D.C.20231  
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

<b>Date of mailing</b> (day/month/year) 18 April 2000 (18.04.00)	
<b>International application No.</b> PCT/GB99/03071	<b>Applicant's or agent's file reference</b> PHM 70390/WO
<b>International filing date</b> (day/month/year) 15 September 1999 (15.09.99)	<b>Priority date</b> (day/month/year) 19 September 1998 (19.09.98)
<b>Applicant</b> MORTEN, John, Edward, Norris	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:  
17 March 2000 (17.03.00)

☐ in a notice effecting later election filed with the International Bureau on:

2. The election ☒ was

☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO  
34, chemin des Colombettes  
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer

Olivia RANAIVOJAONA

Telephone No.: (41-22) 338.83.38

## PATENT COOPERATION TREATY

PCT

NOTIFICATION OF THE RECORDING  
OF A CHANGE(PCT Rule 92bis.1 and  
Administrative Instructions, Section 422)

From the INTERNATIONAL BUREAU

To:

GILES, Allen, Frank  
AstraZeneca  
Global Intellectual Property  
P.O. Box 272  
Mereside, Alderley Park  
Macclesfield, Cheshire SK10 4GR  
ROYAUME-UNI

<b>Date of mailing (day/month/year)</b> 28 September 2000 (28.09.00)	<b>IMPORTANT NOTIFICATION</b>
<b>Applicant's or agent's file reference</b> PHM 70390/WO	
<b>International application No.</b> PCT/GB99/03071	<b>International filing date (day/month/year)</b> 15 September 1999 (15.09.99)

## 1. The following indications appeared on record concerning:

☐ the applicant ☐ the inventor ☒ the agent ☐ the common representative

Name and Address

GILES, Allen, Frank  
AstraZeneca UK Limited  
Global Intellectual Property  
Mereside, Alderley Park  
Macclesfield  
Cheshire SK10 4TG  
United Kingdom

State of Nationality

State of Residence

Telephone No.

01625/516573

Facsimile No.

01625/583358

Teleprinter No.

## 2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

☐ the person ☐ the name ☒ the address ☐ the nationality ☐ the residence

Name and Address

GILES, Allen, Frank  
AstraZeneca  
Global Intellectual Property  
P.O. Box 272  
Mereside, Alderley Park  
Macclesfield, Cheshire SK10 4GR  
United Kingdom

State of Nationality

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Telephone No.

01625/516573

Facsimile No.

01625/583358

Teleprinter No.

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☒ the International Preliminary Examining Authority ☐ other:

The International Bureau of WIPO  
34, chemin des Colombettes  
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer

Athina Nickitas-Etienne

Telephone No.: (41-22) 338.83.38



## PATENT COOPERATION TREATY

PCT

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To:

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Mereside, Alderley Park  
Macclesfield, Cheshire SK10 4GR  
ROYAUME-UNI

<b>Date of mailing</b> (day/month/year) 28 September 2000 (28.09.00)	<b>IMPORTANT NOTIFICATION</b>
<b>Applicant's or agent's file reference</b> PHM 70390/WO	
<b>International application No.</b> PCT/GB99/03071	<b>International filing date</b> (day/month/year) 15 September 1999 (15.09.99)

## 1. The following indications appeared on record concerning:

☒ the applicant      ☐ the inventor      ☐ the agent      ☐ the common representative

## Name and Address

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## Name and Address

ASTRAZENECA AB  
S-151 85 Södertälje  
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## State of Nationality

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☒ the receiving Office      ☐ the designated Offices concerned  
☐ the International Searching Authority      ☒ the elected Offices concerned  
☒ the International Preliminary Examining Authority      ☐ other:

<b>The International Bureau of WIPO</b> 34, chemin des Colombettes 1211 Geneva 20, Switzerland  Facsimile No.: (41-22) 740.14.35	Authorized officer  <b>Athina Nickitas-Etienne</b>  Telephone No.: (41-22) 338.83.38
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